

REMARKS

Claims 1-9 and 11 are pending in the instant application. Claims 1-9 and 11 have been rejected. After entry of these arguments, Claims 1-9 and 11 will remain pending.

Rejection of Claims 1-9 and 11 under 35 USC §103(a)

The Examiner has rejected Claims 1-9 and 11 under 35 U.S.C. §103(a), as allegedly being unpatentable over Bayly et al. (WO 03/075836). Specifically, the Examiner objects to the inclusion of supporting data without naming the source of said data. Additionally, the Examiner does not believe that the closest examples from Bayly were used as relevant comparisons.

Applicants respectfully traverse this rejection. Drug discovery and design is a complex process, and the activity of seemingly similar compounds can be significantly different when tested. Although the compounds of the instant invention are structurally similar to those in Bayly et al., the compounds of the instant invention have improved selectivity over cathepsin S when compared to representative compounds in Bayly et al. Applicants are submitting the declaration of Cameron Black, PhD to support this assertion.

The compounds of the instant invention are amide-substituted peptide nitriles that are useful as selective inhibitors of cathepsin K. The alkyl spacing between the biaryl group and the amide moiety unexpectedly results in a favorable profile when compared to analogues wherein the biaryl group is directly bonded to the amide moiety. As explained in Dr. Black's declaration, the compounds of the instant invention have improved selectivity over cathepsin S when compared to representative compounds in Bayly et al. Dr. Black explains that selectivity is assessed by comparing the IC<sub>50</sub> vs. cathepsin S to the IC<sub>50</sub> vs. cathepsin K. Achieving high levels of selectivity over cathepsin S inhibition was a primary objective of Dr. Black and his team's research and is important due to the known effects on the immune system found in mice with a cathepsin S gene deletion (see, e.g. Driessen et al, *J Cell Biol.*, **147**, 775, 1999; Nakagawa et al, *Immunity*, **10**, 207, 1999).

The observed increase in selectivity exhibited by compounds of the instant invention could not have been predicted, and was not taught by Bayly et al.

In light of these arguments, Applicants respectfully request the rejections of Claims 1-9 and 11 under 35 USC §103(a), be withdrawn.

Provisional Double Patenting Rejection

The Examiner has provisionally rejected Claims 1-9 and 11 on the ground of non-statutory obviousness-type double patenting as being unpatentable over at least claims 1 and 15 of copending Application No. 12/082,104. As this rejection is a provisional rejection based upon pending applications which are still undergoing prosecution, and wherein no allowable subject matter has yet been identified, Applicants respectfully request that this rejection be held in abeyance.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

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